galactosyl epitope. Various labels can be used such as radioisotopes, enzymes, fluorescers, chemiluminescers, particles, etc. There are numerous commercially available kits providing labeled anti-hIg, which may be employed in accordance with the manufacturer's protocol.

For screening the agents for cytotoxic effects, a wide variety of protocols may be employed to ensure that one has the desired activity. One will normally use cells, which may be naturally occurring or modified, cell lines, or the like. The cells may be prokaryotic or eukaryotic. For example, if one is interested in a pathogen, where it does not matter to which epitope the agent conjugate binds, one can combine the pathogenic cells with each of the agents in the presence of an antibody dependent cytotoxic system to determine the cytotoxic effect. One may perform this assay either prior to or subsequent to determining the effect of the various candidate agents on cells of the host to whom the agent would be administered. In this way, one would obtain a differential analysis between the affinity for the pathogenic target and the affinity for host cells which might be encountered, based on the mode of administration.

In some situations, one would be interested in a particular cellular status, such as an activated state, as may be present with T cells in autoimmune diseases, transplantation, and the like. In this situation one would first screen the agents to determine those which bind to the quiescent cell, and as to those agents which are not binding to the quiescent cells, and screen the remaining candidate agents for cytotoxicity to the activated cells. One may then screen for other cells present in the host which might be encountered by the agents to determine their cytotoxic effect. Alternatively, one might employ cancer cells and normal cells to determine whether any of the agents have higher affinity for the cancer cells, as compared to the normal cells. Again, one could screen the library of agents for binding to normal cells and determine the effect.

Those agents which are not cytotoxic to normal cells could then be screened for their cytotoxic effect to cancer cells. Even where some cytotoxicity exists for normal cells, in the case of cancer cells, where there is a sufficient differentiation in cytotoxic activity, one might be willing to tolerate the lower cytotoxicity for normal cells, where the agent is otherwise shown to be effective with cancer cells.

Instead of using cells which are obtained naturally, one may use cells which have been modified by recombinant techniques. Thus, one may employ cells which can be grown in culture, which can be modified by upregulating or downregulating a particular gene. In this way, one would have cells that differ as to a single protein on the surface. One could then differentially assay the library as to the effect of members of the library on cells for which the particular protein is present or absent. In this way, one could determine whether the agent has specific affinity for a particular surface membrane protein as distinct from any of the proteins present on the surface membrane.

One may differentiate between cells by using antibodies binding to a particular surface membrane protein, where the antibodies do not initiate the complement dependent cytotoxic effect, for example, using different species, isotypes, or combinations thereof. By adding the antibodies, blocking antisera or monoclonal antibodies, to one portion of the cells, those cells will not have the target protein available for binding to the library member. In this way one creates comparative cells which differ in their response based on the unavailability in one group of a single protein. While antibodies will usually be the most convenient reagent to use, other specific binding entities may be employed which provide the same function.

For use in the assay to determine binding, one may use an antibody-dependent cytotoxic system. One could use synthetic mixtures of the ingredients, where

only those components necessary for the cytotoxic effect are present. This may be desirable where components of blood or plasma may adversely affect the results of the assay.

Also, while a cellular lawn is an extremely convenient way to screen large numbers of candidates, other techniques can also be used in accordance with the present invention. These techniques include the use of multiwell plates, and the various devices used for the preparation of the combinatorial library, such as pins, tea bags, etc. One may grow the cells separately in relation to the nature of the various devices, where the device may then be contacted with the cells or have the cells grown on the device. The device may be immersed in an appropriate culture, seeded with the cells, or otherwise provided for contact between the cells and the candidate agent. After adding the cytotoxic agent, one may then analyze for lysis in a variety of methods well-known in the art.

In addition, one may wish to know whether the agent has agonist or antagonist activity. The subject assay techniques provide for a rapid way for determining those agents present in the library which bind to the target protein. Once one has substantially narrowed the number of candidate agents, one can use more sophisticated assays for detecting the activity of the agent itself. In this way, one can perform a rapid screen to determine binding affinity and specificity, followed by a more intensive screen to determine activity. Various techniques exist for determining activity, where the cells may be modified, so that a marker gene will be activated which will provide for a detectable signal. Conveniently, the signal may be associated with production of a dye, the production of a surface membrane protein which can be detected with labeled antibodies, or the secretion of a protein which can be detected in the supernatant by any of a variety of techniques. For example, the gene that is expressed may be luciferase modified to have a leader sequence so as to be